is the intralesional injection of bleomycin sulfate. In a series involving more than 1,000 warts, Shumack and Haddock found a 93 percent cure rate within four weeks. A 0.1 percent solution was used, with the volume limited to 0.1 ml in any individual site, with no total dose larger than 2 mg. The major side effects are moderate local pain and burning at the injection site and local pigmentary changes.

These two treatments are important additions to the armamentarium of therapy for recalcitrant human warts. They each have above-average cure rates but should nonetheless be reserved for carefully selected cases because they are not without drawbacks in terms of cost and discomfort to patients. LYLE J. RAUSCH, MD, PhD

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Pemphigus: An Autoimmune Mucocutaneous Disease

PEMPHIGUS IS AN intraepidermal blistering disease occurring on skin and mucous membranes (for example, the mouth, esophagus and vagina). It is the result of loss of normal cohesion between epidermal cells. The findings of recent studies in two aspects of pemphigus have important clinical implications: compelling evidence suggesting the pathogenetic role of pemphigus autoantibodies and evidence of drug-induced pemphigus.

The evidence supporting the pathogenetic role of the pemphigus autoantibodies has been the correlation of pemphigus antibody titers in serum and the activity of the disease; the observation of neonatal pemphigus passively transferred from an affected human mother, and the finding that organ cultures of specimens of normal human skin in the presence of pemphigus antibody developed histologic changes similar to that of naturally occurring pemphigus. Added to the above evidence is the report in 1982 of success in passive transfer of pemphigus from human to laboratory animals. The results of the experiments using intraperitoneal injection of neonatal mice with various concentrations of serum from patients with pemphigus indicate a direct relation between the degree of acantholysis with the titer of pemphigus antibody. In 1982 the antigen(s) to which pemphigus antibodies bind has been characterized as a cell-surface glycoprotein synthesized by human and mouse keratinocytes. Thus, investigations in recent years have convincingly established pemphigus as an autoimmune disease.

The in vitro studies in recent years also provide a great deal of evidence suggesting that pemphigus antibody, in the absence of complement, activates a proteolytic enzyme(s) that in turn causes the destruction of normal cell-to-cell cohesion. Pemphigus appears to be a unique type of autoimmune epidermal injury that does not require the participation of complement.

The clinical importance of these new findings is that the therapy should be directed primarily at reducing the level of pemphigus antibody in affected patients. The administration of systemic corticosteroids and immunosuppressive agents is (still) the treatment of choice. Other modalities of reducing pathogenetic antibodies such as plasmapheresis have been attempted and require further investigation.

D-Penicillamine-induced pemphigus has been increasingly observed—49 cases have been reported in the literature, most of them in the past five years. These cases have characteristic histologic and immunofluorescent features of pemphigus and a close time sequence between the penicillamine administration and the onset of the disorder. This is another example of a drug-induced autoimmune disease though its mechanism is unknown at the present time. The widespread use of penicillamine for connective tissue disorders indicates the monitoring of its side effects should include pemphigus. CHUNG-HONG HU, MD

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Pyoderma Gangrenosum

PYODERMA GANGRENOSUM is an ulcerative skin disorder of unknown cause. Since its description in 1930, little progress has been made in our understanding of the pathogenesis of this disease. However, cumulative clinical experience has provided much information about diagnosis, disease associations and treatment.

The earliest recognizable lesion in this disease is an erythematous papule, nodule or pustule. This early lesion subsequently ulcerates and may enlarge rapidly in a few days until arrested by therapy, it may progress for a longer time—from weeks to months—or it may spontaneously involute. An established ulcer is recognized by its edematous, violaceous and serpiginous border. The ulcer enlarges peripherally and is characteristically undermined at the margin of diseased and normal skin. Lesions most commonly affect the lower extremities, though all body sites can be involved. Lesions characteristically develop at sites of trauma (for example, biopsy sites).

An association between pyoderma gangrenosum and ulcerative colitis is well established. When these two disorders occur together the activity of the skin disease usually parallels that of the bowel disease. Associations between pyoderma gangrenosum and classic rheumatoid arthritis, a seronegative rheumatoidlike arthritis and the arthritis of inflammatory bowel disease have been recognized. Other important but less common disease associations include regional enteritis (Crohn's disease), chronic active hepatitis, plasma cell dyscrasia, leukemia and myeloproliferative syndromes. Pyoderma

gangrenosum occurs without an apparent disease association in about half the cases.

The diagnosis is clinical and rests on the morphologic appearance of an ulcer, its clinical behavior and the presence of an associated disease. Histopathologic findings are not diagnostic but provide supportive evidence for a diagnosis. A biopsy in suspected cases is essential to rule out other mimicking disorders (for example, deep mycoses and atypical mycobacterial infections). Immunofluorescent study of biopsy specimens from an ulcer margin has shown perivascular deposition of IgM, C3 and fibrin in a number of cases. The specificity of this finding and its ultimate use as a diagnostic tool have yet to be established.

Local ulcer care, including careful debridement, and elevation and rest of the affected site are important. Antibiotic therapy should be directed at any associated infection; administration of systemic corticosteroids is the most effective form of treatment. High doses of prednisone, in the range of 80 to 120 mg a day, are frequently required. Sulfones and sulfapyridine are useful for treating steroid-resistant disease or for use as steroid-sparing agents in chronic recurrent disease. Clofazimine, an antimycobacterial agent with antiinflammatory properties, and immunosuppressive agents, particularly azathioprine, have also been used successfully in recalcitrant cases.

ROBERT A. SNYDER, MD

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Warts Are Important, Too

HUMAN PAPILLOMAVIRUS is capable of producing a number of clinically distinct epithelial neoplasms. Previously these clinical characteristics were thought to be determined by the anatomic site where the wart developed, rather than by the virus itself. With improvements in immunofluorescence and immunoperoxidase technology, it appears that there are as many as eight immunologically distinct human papillomaviruses. To a large extent, their antigenic differences reflect their clinical appearance. For example, papillomavirus types 1 and 4 are associated with plantar warts, type 2 with common warts, type 3 with flat warts, type 6 with genital warts and type 7 with butcher's warts.

Papillomavirus type 5 is associated with a rare familial disease called epidermodysplasia verruciformis. In those afflicted, warty neoplasms develop over much of the skin. These tumors tend to degenerate into squamous cell carcinoma. Recently, using DNA hybridization techniques, DNA sequences characteristic of papillomavirus type 5 have been found in a number of squamous cell carcinoma lesions from such patients.

Others have linked genital warts (type 6) with cervical cancer. On the basis of histologic evidence, an unusual condition of the cervical epithelium has been described that is believed to be due to a "subclinical infection" by the papillomavirus. There is compelling statistical evidence that this histologic change is causally related to cervical neoplasia.

Bowenoid papulosis of the genitalia is a newly recognized neoplasm consisting of multiple 3- to 10-mm pigmented papules on the external genital. Because of its disturbing histologic appearance, there is concern over its malignant potential. Both ultrastructural and immunologic evidence has recently pointed to the existence of papillomavirus in these lesions.

Further investigation into host-parasite relationships in papillomavirus-induced neoplasms should be productive. At the very least, we have learned that the wart is not in the least bit "common."

GARY W. COLE, MD

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Dysplastic Nevus Syndrome

DYSPLASTIC NEVI were first reported to occur in association with familial malignant melanoma, which accounts for 1 percent to 6 percent of the total cases of melanoma. The presence of such atypical nevi has been designated the "B-K mole" syndrome based on the initials of the surnames of two families originally studied. These lesions occurred in 18 of 20 (90 percent) patients with familial melanoma and 24 of 43 (56 percent) first-degree relatives. Since this report, the occurrence of dysplastic nevi has also been observed in patients with nonfamilial melanoma. As clinical and histologic features of dysplastic nevi in a familial or sporadic context are similar, the following nomenclature has been proposed: dysplastic nevus syndrome, sporadic type, or dysplastic nevus syndrome, familial type. Recognition of such precursor lesions to melanoma may serve to identify patients at risk for this malignancy. Careful follow-up with photographic documentation and biopsy of lesions suggesting malignant transformation are important so that lesions may be surgically removed at an early, curable stage.

Characteristically, dysplastic nevi are larger in size (more than 5 mm) than ordinary acquired nevi and have an irregular color and outline. Although shades of tan or brown predominate, there may be pinkish hues and slight scaling depending on the degree of inflammation. Dysplastic nevi range in number from a single lesion to 200 or more, and occur on covered as well as sun-exposed areas of the body. Lesions continue to develop throughout adult life. Histologic features include atypical intraepidermal melanocytic hyperplasia, dense dermal lymphocytic infiltration with fibroplasia and increased vascularity.

A polygenic inheritance of precursor nevi has been proposed because of the large number of affected persons in melanoma-prone families and the high fre-